Remarks

Claims 42, 45, 46, and 51-62 were pending in the subject application. By this Amendment, claim 1 has been amended and new claim 63 has been added. Support for the new claim and amendment can be found throughout the subject specification and in the claims as originally filed. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 42, 45, 46, and 51-63 are currently before the Examiner for consideration. Favorable consideration of the pending claims is respectfully requested.

Claims 42, 45, 46, and 51-62 are rejected under 35 USC §112, first paragraph, as non-enabled by the subject specification. The Examiner acknowledges that the specification enables inhibiting expression of DV genes within an isolated host cell by RNA interference; however, the Examiner asserts that the specification does not enable inhibition of expression of DV genes in a host animal. The Examiner also asserts that delivery of gene expression vectors *in vivo* is problematic. Applicants respectfully assert that the claims are enabled by the subject specification. A person of ordinary skill in the art would expect that inhibition of expression of DV genes in a mammalian host animal can be achieved using the claimed method. The inhibition of expression of DV genes in a host cell correlates with inhibition of expression of DV genes in a mammalian host. In addition, the subject specification teaches the appropriate target cells for delivery of the vector. Moreover, the vector can be delivered to appropriate cells *in vivo* using standard methods and materials known in the art. For example, when the vector is administered with chitosan nanoparticles by a mucosal route, the vector nanoparticles are primarily taken up by dendritic cells and macrophages, which are the cells where Dengue virus replicates. Thus, the ordinarily skilled artisan, having the benefit of the teachings of the subject application, knows to which cells in a mammal that the vector should be delivered and can deliver the vector to those cells *in vivo*.

Applicants also disagree with the assertion by the Examiner that the delivery of gene expression vector *in vivo* is problematic. There are numerous successful reports of safe and effective gene delivery *in vivo* and several advanced clinical trials in progress. Moreover, the references cited by the Examiner as evidence of lack of enablement of gene therapy do not represent the state of the art at the time of the filing of the subject application (February 21, 2003). The cited references range

in publication date from 1997 to 2003. The state of the art for gene therapy at the time of the filing of the subject application has advanced considerably farther than it was in 1997, 2000, or even 2003. Accordingly, Applicants respectfully assert that the claimed method is enabled by the subject specification. Reconsideration and withdrawal of the rejection under 35 USC §112, first paragraph, is respectfully requested.

Claims 42, 45, 46, 52, 53, 55, 58, and 59 are rejected under 35 USC §103(a) as obvious over Raviprakash *et al.* (1995) in view of Adelman *et al.* (2002), Tuschl *et al.* (U.S. Patent No. 7,056,704), and Yu *et al.* (2002). Claims 54, 57, 61, and 62 are rejected under 35 USC §103(a) as obvious over the same references as cited above, further in view of Adelman *et al.* (2001), Yu *et al.* (U.S. Patent No. 6,852,528), and Kumar *et al.* (U.S. Patent No. 7,067,633), respectively. The Examiner cites the Raviprakash *et al.* reference as teaching inhibiting expression of DV gene products in mammalian cells *in vitro* and Adelman *et al.* is cited as teaching siRNA vectors to DV RNA. Applicants respectfully traverse these grounds of rejection.

Applicants respectfully assert that the cited references, taken alone or in combination, do not teach or suggest the claimed invention. By this Amendment, Applicants have amended claim 42 to recite that DV gene expression is inhibited in a mammalian animal host. As the Examiner acknowledges, the Raviprakash *et al.* reference only discloses inhibition of DV gene product in mammalian cells *in vitro*. There is no teaching or suggestion of inhibition of DV gene expression *in vivo* in a mammalian animal. As the Examiner is aware, the combination of cited references must teach or suggest each and every element and limitation contained in the rejected claim. The references cited by the Examiner fail to teach or suggest each and every element of Applicants' claimed invention.

Moreover, as the Examiner acknowledges, the Raviprakash *et al.* reference does not teach a vector encoding an siRNA that reduces expression of a target DV gene by RNA interference. The secondary references fail to cure this deficiency. Nor do any of the cited references teach or suggest the use of tissue-specific or inducible promoters operably linked to an siRNA encoding polynucleotide. The Examiner asserts that the use of such promoters is a "matter of design choice." Applicants respectfully assert that it is only through impermissible hindsight reconstruction that a

person of ordinary skill in the art would be able to select appropriate tissue-specific or inducible promoters for use in Applicants' claimed invention.

As the Examiner is aware, in order to support a *prima facie* case of obviousness, a person of ordinary skill in the art must generally find both the suggestion of the claimed invention, and a reasonable expectation of success in making that invention, solely in light of the teachings of the prior art and from the general knowledge in the art. *In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). One finds neither the suggestion, nor the reasonable expectation of success, of Applicants' claimed invention in the cited references. Thus, Applicants respectfully assert that the claimed method is not obvious over the cited references. Accordingly, reconsideration and withdrawal of the rejections under 35 USC §103(a) is respectfully requested.

It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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